The Surgical Clinics of North America
April, 1956. Volume 36, Number 2
Published by W. B. Saunders Company

Certain Methods for Artificial Support of the Circulation During Open Intracardiac Surgery

CLARENCE DENNIS, M.D., PH.D., F.A.C.S.*

IN THE middle 1930's, before the electrification of medical thought produced when Robert Gross tied his first patent ductus arteriosus,[1] when Gross[2] and Crafoord[3] repaired their first coarctations of the aorta, and when Blalock[4] performed his first subclavian-pulmonary anastomosis for tetrology of Fallot, the nidus of a highly imaginative idea was born in the mind of John H. Gibbon, Jr., of Philadelphia.[5] Gibbon's idea revolved about the creation of apparatus and techniques which would make possible diversion of caval blood returning to the right heart, passage of it through artificial heart and lungs, and return of it to the aorta. He reasoned that such a method should enable the surgeon to operate upon intracardiac anomalies under direct vision in a relatively dry field, while the brain, myocardium and liver, together with other tissues, receive adequate flows of oxygenated blood.

Since that time, remarkable strides have been made in pursuit of Gibbon's objective, a major share of which have been made by Gibbon himself, his immediate associates, and groups who have applied the lessons he has taught.

The author's group embarked upon the pump-oxygenator field in 1947, having been provided encouragement and orientation by Gibbon. Slightly earlier, Björk[6] had undertaken to study this field under the stimulus of Crafoord in Stockholm. After preliminary reports began to appear from these groups, and after the full impact of the advances made by Gross, Blalock and Crafoord, numerous other groups recognized the

From the State University of New York College of Medicine at New York City and the Surgical Service, University Division, Kings County Hospital, Brooklyn, New York.

** Professor and Chairman, Department of Surgery, State University of New York College of Medicine at New York City; formerly Professor, Department of Surgery, University of Minnesota.*

handicaps imposed by the inability of the surgeon safely to view and to handle the interior of the heart, and began to report work in this field.

Simultaneously, workers in related areas opened new horizons. Two of these contributions were the use of the atrial well technique by Gross,[7] and the use of refrigeration, the idea of which was introduced by Bigelow,[8] but the first successful clinical application of which was that of Lewis and Taufic.[9]

A closely related innovation arose from the observation of Andreason and Watson[10] that dogs tolerate well for 30 minutes occlusion of caval flow to the heart provided only that the azygos vein return be left open. The flows which take place under these circumstances amount to approximately 15 ml. per minute per kilogram of body weight, in contrast to 100 to 160 ml. in the normal state. This "azygos principle" has been utilized by Lillehei, Cohen, Warden and Varco[11, 12] in the various techniques which they and their associates have so brilliantly employed. The facilitation of these accomplishments appears to have rendered unnecessary the early goal of Gibbon, the author, and other workers in the pump-oxygenator field, namely, the turnover of blood by the extracorporeal circuit in normal volume and with maintenance of normal pressure relationships.

The purpose of the present paper is to outline in broad form those aspects of these developments with which the author is most conversant.

REQUIREMENTS OF A SATISFACTORY APPARATUS TO PERMIT OPEN INTRACARDIAC SURGERY

1. Substitution for Lungs as Well as Heart

Early in the development of this field, Sewell and Glenn,[13] Wesolowski and Welch,[14] and Sirak and his associates[15] undertook to perform multiple incannulations to permit use of the lungs of the subject during open cardiotomy. This of necessity requires occlusion of pulmonary venous return in addition to incannulation of both venae cavae, the pulmonary artery, the pulmonary venous return, and the aorta. These cumbersome manipulations have been so discouraging that all have accepted the requirement that the extracorporeal circuit accomplish the work of the lungs as well as that of the heart during the period of perfusion, thus eliminating the pulmonary arterial and the pulmonary venous incannulations.

2. Adequate Extracorporeal Gas Exchange

The introduction of oxygen and the elimination of carbon dioxide are known not to be the sole functions of the lung, but the work of many groups has been based on the supposition that elimination of the other

functions is probably not of importance for the short duration of the operative intervention on the heart.

The actual gas exchange has in various centers been accomplished by (*a*) exposing a flowing film of blood to an oxygen atmosphere, (*b*) bubbling oxygen through blood, (*c*) perfusing blood through the excised lung of a laboratory animal, and (*d*) perfusing the blood of the subject through the circulation of an intact individual of the same species.

Each of these methods presents advantages and problems. The last named method is regarded as safest for the patient by Lillehei and his associates,[16] but it exposes an additional subject to risks which they wish to avoid. Use of an animal lung for oxygenation for a human subject has proved successful in the hands of Mustard (macaque lung) and of Campbell[17] (dog lung) and their associates, but it entails extensive and time-consuming manipulations and at least theoretical dangers of contamination.

Use of a bubble-type oxygenator has been favored by many groups (Gollan,[18] deWall,[19] Gimbel[20]). The elimination of bubbles, once formed, has been attempted by many techniques, and appears actually to have been accomplished. The risks of gas embolization, as expanded below, have led the author's group to concentrate upon use of a flowing film.

In the oxygenation of blood by exposure of a thin film to a high oxygen atmosphere, it is essential to use a wettable surface on which to form the blood film. Oxygenation has been most effective if the film has been less than 0.3 mm. thick and has been permitted to flow over a steel mesh to accomplish mixing during exposure. Stationary screen has been used for this purpose by Gibbon, but the tendency of the blood film to break down if the blood flow is temporarily stopped has necessitated an additional inner circuit in the apparatus to maintain the film.

The author's group has employed a disk of steel screen 20 inches in diameter which rotates 24 times a minute in an oxygen atmosphere on a horizontal shaft. Blood drops a few millimeters from the dependent margin of the disk, and collects in a small reservoir for return to the aorta of the subject. The film produced by laying blood on the central portion of the disk is not only stable under these circumstances, but dry disks film spontaneously in a matter of seconds, if more oxygenating capacity is desired while the apparatus is in use. Each such disk is capable of fully saturating normal venous blood at a rate in excess of 500 ml. per minute. With four disks placed in the oxygenator, the maximum flow which has been used clinically is 2200 ml. per minute. This was adequate to permit cardiotomy with closure of a septal defect and cure in a young adult.

3. Efficient Pumps

In general the circuit must have a minimum of moving parts, and maximal freedom from profound pressure and velocity gradients. Piston

pumps are productive of excessive hemolysis, and the patterns which have found favor in various laboratories are: (*a*) the Dale-Schuster pattern, (*b*) the DeBakey pattern, (*c*) the finger pump, (*d*) open air-pressure patterns and (*e*) gravity alone.

(*a*) The Dale-Schuster pattern is one in which at least a portion of a pump chamber is composed of flexible material, which can be activated by alternating fluid, gas, or mechanical pressure.[21] Directional flow has in most instances been facilitated by unidirectional valves activated by the changing pressures in the blood. This pattern we have employed because of the minimization of hemolysis, and the simplicity, automaticity and safety of the control of the blood volume in the apparatus.

(*b*) The DeBakey pattern is essentially one in which rollers compress a flexible tube to cause the contained blood to move.[22] Inclusion of simple mechanisms to control such pumps has not been accomplished as yet.

(*c*) Finger pumps* resemble the DeBakey arrangement except that compression of the tubing is accomplished in progressive coordination by a series of mechanical fingers. Finger pumps and DeBakey pumps enjoy freedom from the need of valves.

(*d*) Leland Clark and his associates have developed an air pressure pump in which the pressure is applied above a blood-gas interface in a closed chamber. Valves are required to give directional flow, and an electronic circuit is needed for controlling the intermittently positive pressure above the blood surface.

(*e*) As first suggested by Karlson,[23] perhaps the simplest solution is an elevated reservoir, the blood being perfused through the subject a single time, perhaps utilizing only the force of gravity to drive it. Such a method has been used clinically by Lillehei and his associates,[16] utilizing the reduced flows they have found adequate, with gratifying results. The limitation of time implied is the chief deterrant. It has been reserved for infants to date, chiefly because of the volumes of blood required for larger patients.

Until the introduction of the "azygos flow principle" by Andreason and Watson[10] and the expansion of it by Cohen and Lillehei,[11, 12] the flows maintained were thought to be properly equivalent to normal for the body weight involved. Therefore all early groups aimed at flows in the neighborhood of over 100 ml. per minute per kilogram of body weight. Dennis, Varco, et al.,[25] indeed, used a flow in excess of 220 ml. per minute per kilogram in their first case, apparently the first in which perfusion techniques were applied to operative correction of congenital defects. Use of the smaller flows introduced by Lillehei, Cohen, Warden and Varco[12] minimizes the risks of air embolism, thrombin embolism,

* Manufactured by the Sigma-Motor Corp., Middleport, New York.

and hemolysis, and permits low systemic pressures during cardiotomy, which vastly reduce blood loss and replacement needs.

This Minneapolis group sets the arterial flow to predetermined levels, usually about 50 ml. per minute per kilogram of body weight, and governs the venous drainage to match. The author's group permits venous drainage by gravity and governs arterial return to the subject quantitatively to maintain a constant volume of blood in the extracorporeal circuit, adding new blood to the arterial side if flows fall below predetermined levels. Gibbon, and Kirklin and Wood[26] have pumped blood from the cavae and maintained a constant extracorporeal volume, adjusting the withdrawal flows to desired levels; more recently they have utilized a refined gravity drainage. Which is the most satisfactory method remains to be seen.

4. Control of Clotting

Hemostasis in the subject is favored by the rapid coagulation of shed blood or blood in injured vessels. The types of apparatus mentioned herein, however, require that such clotting be impeded, lest thrombin emboli be returned to the circulation of the subject or plug the filters or other portions of the extracorporeal circuit. Citrate in adequate amount is not acceptable, because of the effect of this agent upon the myocardium, partially through changes in calcium ion concentration. Use of ion exchange calcium removal in the circuit has not as yet been successful in the laboratory. All groups currently employ heparinization for prevention of clotting in the apparatus during perfusion, and most utilize protamine for neutralization of the heparin effect when perfusion has been completed.

There is variation in findings in relation to the control of clotting. In the author's group, it has been necessary to raise the heparin level to 50 to 60 micrograms per ml. during perfusion to prevent formation of fibrin in the oxygenator or other parts of the apparatus. Protamine administration has been controlled by frequently repeated protamine titrations and has been accomplished over a period of 15 minutes, inasmuch as peripheral vasodilatation apparently occurs following rapid injection of the drug, producing hypotension and persistent oozing of the operative area. This complication of protamine administration has not been the experience in Minneapolis and at the Mayo Clinic, and the explanation for the dissimilar findings has not yet been found.

An additional problem in relation to coagulation of the blood is related to changes in the clotting mechanism not apparently directly related to the use of heparin and protamine. There is a loss of platelets in passage of blood through all the artificial oxygenators in which platelets have been studied. There is apparently also some loss of fibrinogen, although data in this regard are inconclusive. The quality of the clot following

perfusion in dogs is prone to be poor in that the clot fails to retract or is easily broken up or actually redissolved on shaking the test tube in which it has formed. The development of fibrinolysin under these circumstances demands more study.

From a practical point of view, the problem in dogs is most effectively handled in our laboratory by slow back-titration with protamine followed by direct blood transfusion. Fortunately the clotting problem has appeared to be less troublesome in patients than in dogs.

5. Prevention of Injury to Formed Elements of the Blood

Destruction of the red cell serves as the simplest index of injury to formed elements, as the determination of the plasma hemoglobin concentration is direct and quick. Plasma hemoglobin concentrations up to 200 mg. per 100 cc. are not per se productive of recognized damage to the subject. Minimization of hemolysis has been attained by utilization of certain of the nonwettable synthetic plastic materials to build the apparatus. The chief disadvantage of the open film technique appears therefore to lie in the need for a wettable surface (stainless steel).

Hemolysis also occurs in areas of turbulence or of abrupt changes in velocity and possibly in pressure. Careful control of the diameters of the tubing used, care as to competence of valves, and avoidance of pinchcocks to control rates of flow are all important.

Loss of platelets in the author's laboratory occurs slowly during perfusion, about half disappearing from the system in one hour of total body perfusion in the dog. Loss of white cells concerns principally the segmented polymorphonuclears; the over-all loss is about one-half of the white cells per hour of total perfusion.

The loss of red cells is indicated by rise in plasma hemoglobin, which rises less than 50 mg. per 100 cc. in a half-hour of total perfusion.

Damage to formed elements is now apparently not a problem to those groups doing clinical work.

6. Prevention of Gas Embolus

Accidental injection of air into a peripheral vein is rarely lethal to the dog unless amounts in excess of 30 ml. are given quickly. On the other hand, gas bubbles in the aortic outflow of the heart are lethal in small quantities. Lam and Geoghegan[27] have shown that gas in the coronary arteries is quickly lethal due to arrhythmias or arrest, but that such bubbles can be eliminated by perfusion under pressure, with recovery of the heart. At the laboratory in Brooklyn, continued perfusion has been repeatedly observed to be followed by disappearance of such bubbles and recovery of the myocardium, the driving force for the coronary circulation coming from the heart-lung apparatus during this period of recovery.

As Lam and Geoghegan re-emphasized, the presence of gas bubbles in the cerebral vessels is, under the circumstances under consideration, more lethal than gas in the coronary arteries, and is prone to lead to death after an interval of several hours. My associates have pursued this problem in detail and have learned that injection of less than 1.5 ml. per minute of air or oxygen into the carotid artery of the dog is not infrequently lethal and will occasionally leave no signs which have been recognized at autopsy.[28] Injection may be followed by recovery of consciousness, with development of coma and death 6 to 24 hours later. The clinical findings resemble those seen in acute temporary circulatory cerebral arrest (Baker, Kabat and Dennis[29]).

Tubing in the apparatus may be free of leaks as tested under internal pressure with blood or water, but may permit ingress of atmospheric air into the blood if internal pressures appreciably lower than atmospheric are permitted to exist. Appreciation of the above factors has led us not only to avoid the use of bubble oxygenators, but to redesign the whole apparatus to avoid the presence of pressures lower than atmospheric. In spite of these changes, it has been helpful to include a bubble remover to deal with those few bubbles which result from the few millimeter drop off the oxygenator disks.

7. Minimization of Metabolic Changes

Changes in the acid-base relationships during perfusion are primarily due to changes in carbon dioxide content. In Brooklyn, the oxygenator atmosphere is pure oxygen, and the carbon dioxide tension in the blood is regularly reduced thereby to about 20 mm. of mercury from the normal of 40 mm. Gibbon, and Wood and Kirklin endeavor to retain the pH of the blood at a predetermined level by automatic adjustment of the carbon dioxide content of the atmosphere in the oxygenator. In either case, there appears to be regularly a slow increase in the acidity of the blood due to accumulation of nonvolatile, or fixed, acids. This accumulation is inconsequential for operative clinical purposes as long as adequate flows (40 to 50 ml. per minute per kilogram of body weight) of well oxygenated blood are maintained.

Changes of other constituents in the blood appear to be slight. Concentrations of sodium, potassium and chloride ions have been carefully studied and do not alter appreciably. Through the collaboration of Dr. Kurt Stern, of the Brooklyn Polytechnic Institute, plasmaphoretic studies on the proteins of the blood have been performed in connection with animal perfusions. Such studies on the proteins of the plasma indicate no detectable changes. Studies of certain fixed acids indicate a slight increase. Thus, pyruvic acid concentrations increase to two to three times the control level in many perfusions; those animals with higher rises in general do not survive.

8. Hypothermia, Control of Body Temperature

The addition of refrigeration as a means to broaden the fields to which perfusion techniques might be applicable has been evaluated by the author's group, by Lind and by Gollan. New problems of myocardial arrhythmia are superimposed by such refrigeration, but the possibilities of this combination of techniques have still been inadequately explored.

In clinical work, the body temperature of the subject is currently maintained near normal levels by thermostatic control of the patient, the apparatus, or both.

THE APPARATUS AT STATE UNIVERSITY OF NEW YORK

This apparatus is described because it is that with which the author has most familiarity and because it has worked nicely in four clinical trials. The apparatus is built primarily of methyl methacrylate for machined parts, polyvinyl plastic for tubing, and stainless steel for those portions which must be wettable, which must be autoclaved, and for portions the machining of which must be precise. It is mounted upon a platform 2 or 3 inches off the floor of the operating room in order that blood may flow by gravity from the venae cavae to the apparatus. Blood is filmed upon one to four revolving disks in the oxygenator depending on the flows of blood expected. Each disk is capable of raising the oxygen saturation of normal blood from 50 to 95 per cent at a rate in excess of 500 ml. per minute. The disks are 50 cm. in diameter, made of 18 by 18′ wire mesh, and rotate on a horizontal axis at 24 revolutions per minute. Pure oxygen flows at 11 liters per minute through the oxygenator chamber. The effluent from the oxygenator flows by hydrostatic pressure upward in the central chamber of a bubble trap. This trap is filled with stainless steel scouring sponge coated with Dow-Corning anti-foam. Blood overflows from the top of this column into an outer jacket, which serves as a reservoir, and is then led from the bottom of this reservoir to the pumps. The pumps are made in a modified Dale-Schuster pattern, and are driven by compressed air. The pumping system is self-regulatory and it depends entirely upon gravity for the filling for each stroke of the pumps. The flexible diaphragm of the pumps is activated by compressed air, which in turn is controlled by a small mercury switch, tripped by changes in position in the flexible diaphragm.

Blood is circulated through a shunt from the arterial to the venous segment of the extracorporeal circuit to accomplish complete elimination of bubbles before perfusion of the subject begins. Oxygenator blood is returned to the subject by a cannula placed in the left subclavian artery. Blood is withdrawn from the subject by means of two catheters of as large size as seems easily to fit into the superior and inferior venae cavae, placed through the wall of the right atrium. Rates of flow are measured by a rotameter which records electromagnetically, and which is

placed in the venous flow from the animal to the oxygenator. The rate of arterial flow is apparent to everyone in the operating room by virtue of the audible action of the arterial pumps. Diagrams of the apparatus are shown in Figures 130 to 133.

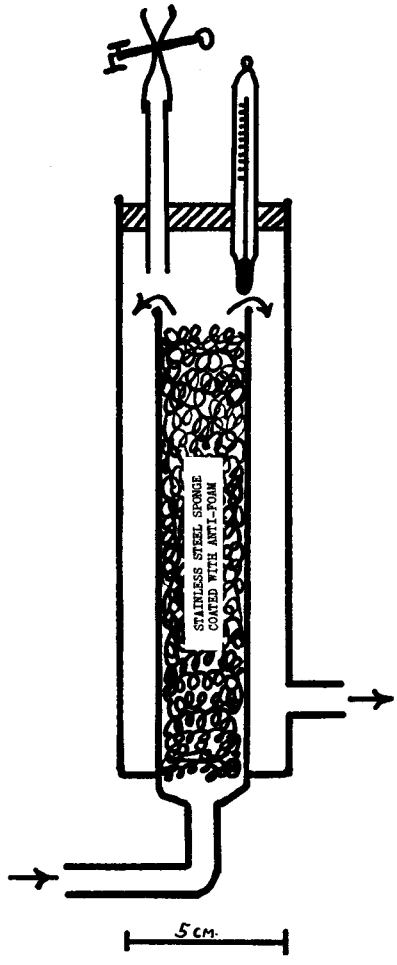

Fig. 130. The bubble trap utilized in the laboratory of the author's group. (From Surgery *38:* 30, 1955.)

CLINICAL ACCOMPLISHMENTS WITH OXYGENATORS

The author and his associates have as yet had little experience with the clinical application of the pump-oxygenator device which they have developed over the past eight years. Two patients were placed upon a previous type of oxygenator in the University of Minnesota Hospitals in the spring and summer of 1951. Neither of the patients was a survivor,

the loss of the first being due to an inadequate supply of heparinized blood and an inadequate orientation with regard to the anatomy of persistent atrioventricular canal. The second was lost through an unfortunate human failure in the course of the perfusion, as a result of which oxygen in quantity was blown into the aorta. The modification of the apparatus which has occurred since that time makes this catastrophe no longer possible.

As Gibbon so richly deserved, he was the first successfully to use a pump-oxygenator for complete deviation of caval blood from the heart to correct an intracardiac congenital defect.[30]

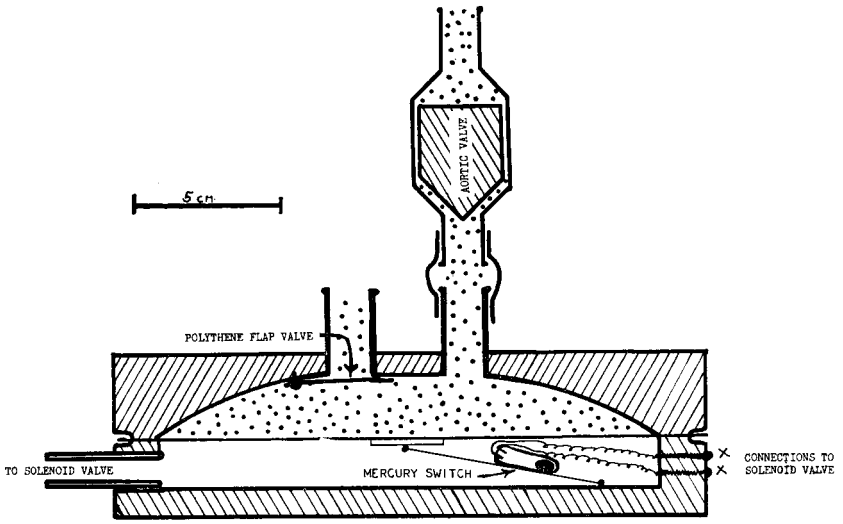

Fig. 131. The modified Dale-Schuster pump. The lever carrying a mercury switch is activated by a flexible rubber diaphragm in such fashion that filling of the chamber above the diaphragm results in closure of an electrical circuit which activates a solenoid valve which in turn compresses the blood-filled chamber so as to pump blood into the arterial system of the subject. At the end of the stroke the mercury switch opens the circuit to permit filling of the blood-containing chamber again. Directional flow is provided by an inlet and an outlet valve. (From Surgery *38:* 30, 1955.)

On November 1, 1954, a patient with trivalvular postrheumatic heart disease and failure resistant to medical management was placed on partial perfusion with this apparatus for a period of four hours at the Kings County Hospital, Brooklyn. In the course of this prolonged perfusion, which was carried out at an average flow of between 700 and 800 ml. per minute, the patient's pulmonary edema and hydrothorax disappeared, and she was so immensely improved as to be relieved of her orthopnea and more than 12 pounds of her edema over a period of more than a week after the perfusion. This case has previously been reported.[31]

Since that time operations in three cases have been undertaken with the aid of the oxygenator. In the first, the author was unsuccessful in avoiding ingress of air through an interventricular septal defect, and it is felt the patient was lost due to this factor. An immense degree of aortic insufficiency flooded the field, leading to the loss of systemic pressure, opening of the aortic valves secondarily, and ingress of air during this period of hypotension. In the second case the right atrium and the right ventricle were both opened for a large interatrial defect and a suspected

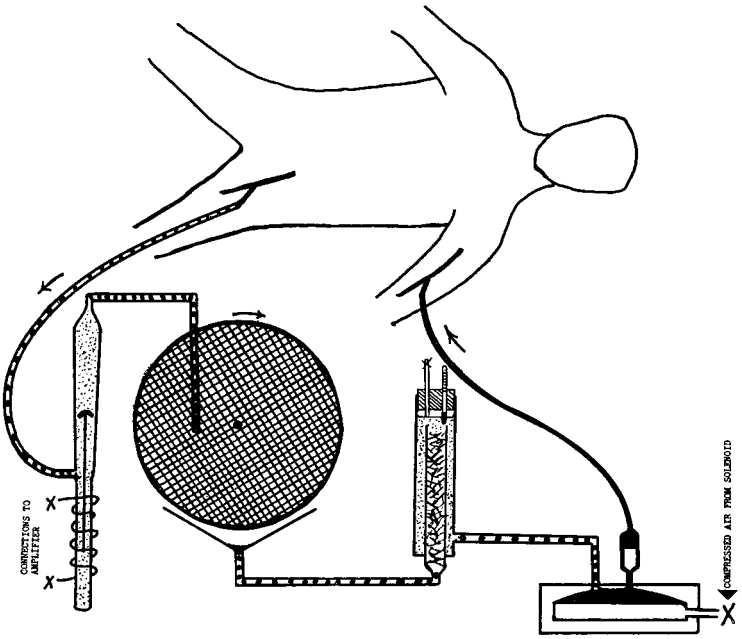

Fig. 132. Schematic drawing of the perfusion apparatus in the management of a patient with a trivalvular postrheumatic cardiac failure resistant to other types of treatment. The connections utilized in the operative management of intracardiac congenital defects vary from those shown in this diagram in that the blood is withdrawn from the superior and inferior venae cavae by way of plastic catheters through the wall of the right atrium, as suggested by Varco and Lillehei. Return is accomplished by a cannula or catheter placed in the left subclavian artery. (From Surgery *38:* 30, 1955.)

pulmonic stenosis. The defect was closed, and the pulmonic stenosis was found not to be present. The patient made an uneventful recovery and apparently is cured. This procedure was performed on June 30, 1955, and will be reported in detail elsewhere. The third patient, an adult, had a huge heart, and a similar defect was diagnosed preoperatively. She was found at operation to have persistent atrioventricular canal, agenesis of much of the tricuspid valve, adhesive postrheumatic pericarditis, and postrheumatic mitral insufficiency. The procedure was performed suc-

cessfully, but it was simply more than this heart could tolerate, and although the perfusion portion of the operation went very nicely, and the patient survived ten hours, the heart did not take over the circulation adequately to maintain her.

One additional patient has been perfused by the elevated reservoir technique in attempted repair of a large interventricular septal defect; perfusion was inadequate in all probability, and the defect was of such large dimension that it is the consensus that it could not have been closed. It was not possible to close it by suture at autopsy.

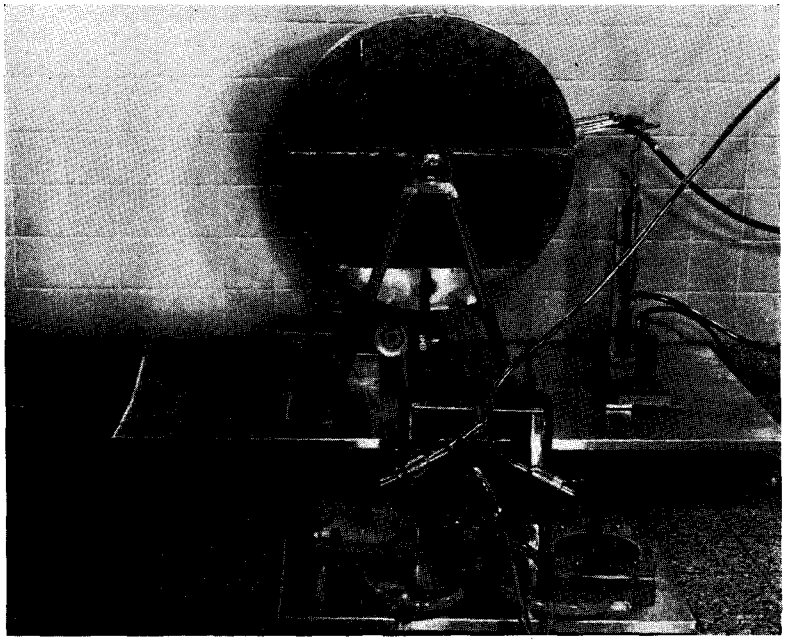

Fig. 133. Photograph of apparatus as it now stands.

The group at the University of Minnesota, headed by Lillehei and Varco, have had more experience than any other in the field of operative surgery with the aid of perfusion techniques. They have, as of the present time, performed more than 75 perfusions of one kind or another for the support of the circulation during open cardiotomy. Initially they utilized a human donor for purposes of cross transfusion, which they have reported elsewhere. Subsequently, in an effort to avoid the utilization of a human oxygenator, or donor, they have utilized other techniques, which have been briefly mentioned in the text above. DeWall, working with them, has recently developed a bubble type of oxygenator which has been utilized on a small number of patients.[19] It appears that this has proved satisfactory, and further evaluation of it is in progress.

Wood, Kirklin and their associates at the Mayo Clinic have utilized a modification of the Gibbon pump-oxygenator on a series currently in excess of 25 patients. Their results have been as brilliantly successful as have those of the group at Minneapolis.

The mortality rates early in the experience of all groups have been and can be expected to be high. The mortality rates have, however, dropped sharply both in Minneapolis and in Rochester, with the gaining of further clinical operative experience. It would appear that the closure of interventricular septal defects can be accomplished in properly selected cases with a risk of less than 10 per cent. The definitive repair (cure) of tetralogy of Fallot now carries a somewhat higher risk, but may well also fall below 10 per cent as more experience is gained. It is essential, however, that extensive laboratory experience with the method by a highly developed and integrated team must precede clinical application of the methods employed. In the hands of such groups there appears to be every reason for optimism concerning the extension of such techniques to more complicated cardiac lesions.

REFERENCES

1. Gross, R. E. and Hubbard, J. P.: Surgical Ligation of a Patent Ductus Arteriosus. Report of First Successful Case. J.A.M.A. *112:* 729, 1939.
2. Gross, R. E. and Hufnagel, C. A.: Coarctation of the Aorta. Experimental Studies Regarding Its Surgical Correction. New England J. Med. *223:* 287, 1945.
3. Crafoord, C. and Nylin, G.: Congenital Coarctation of the Aorta and Its Surgical Treatment. J. Thorac. Surg. *14:* 347, 1945.
4. Blalock, A. and Taussig, H. B.: The Surgical Treatment of Malformations of the Heart in Which There Is Pulmonary Stenosis or Pulmonary Atresia. J.A.M.A. *128:* 189, 1945.
5. Miller, B. J., Gibbon, J. H. Jr. and Gibbon, M. H.: Recent Advances in the Development of a Mechanical Heart and Lung Apparatus. Ann. Surg. *134:* 694, 1951.
6. Björk, V. O.: Brain Perfusions in Dogs with Artificially Oxygenated Blood. Acta chir. Scandinav. *96:* Suppl. 137, 1948.
7. Gross, R. E., Watkins, E. Jr., Pomeranz, A. A. and Goldsmith, E. L.: A Method for Surgical Closure of Interauricular Septal Defects. Surg., Gynec. & Obst. *96:* 1, 1953.
8. Bigelow, W. G., Callaghan, J. C. and Hopps, J. A.: General Hypothermia for Intracardiac Surgery. Ann. Surg. *132:* 531, 1950.
9. Lewis, F. J. and Taufic, M.: Closure of Atrial Septal Defects with Aid of Hypothermia; Experimental Accomplishments and Report of One Successful Case. Surgery *33:* 52, 1953.
10. Andreason, A. T. and Watson, F.: Experimental Cardiovascular Surgery. "The Azygos Factor". Brit. J. Surg. *39:* 548, 1952.
11. Cohen, M. and Lillehei, C. W.: A Quantitative Study of the "Azygos Factor" During Vena Caval Occlusion in the Dog. Surg., Gynec. & Obst. *98:* 225, 1954.
12. Lillehei, C. W., Cohen, M., Warden, H. E. and Varco, R. L.: The Direct Vision Intracardiac Correction of Congenital Anomalies by Controlled Cross Circulation. Surgery *38:* 11, 1955.
13. Sewell, W. H. Jr. and Glenn, W. L.: Experimental Cardiac Surgery. II. Further Observations on the Development of a Perfusion Pump for the Purpose of

Shunting the Venous Return Directly into the Pulmonary Artery. Surgical Forum, Am. Coll. Surgeons, 1950, p. 265. Philadelphia, W. B. Saunders Co., 1951.
14. Wesolowski, S. A. and Welch, C. S.: A Pump Mechanism for Artificial Maintenance of the Circulation. Surgical Forum, Am. Coll. Surgeons, 1950, p. 226. Philadelphia, W. B. Saunders Co., 1951.
15. Sirak, H. D., Ellison, E. H. and Zollinger, R. M.: Cardiotomy into an Empty Left Ventricle. Surgery *28:* 225, 1950.
16. Lillehei, C. W. and Varco, R. L.: Personal communications.
17. Campbell, Gilbert: Personal communication.
18. Clark, L. C. Jr., Gollan, F. and Gupta, V. B.: The Oxygenation of Blood by Gas Dispersion. Science *111:* 85, 1950.
19. deWall, Richard: Personal communication.
20. Gimbel, N. S. and Engelberg, J.: Oxygenator for Use in Heart-Lung Apparatus. Surg. Forum, Am. Coll. Surgeons, 1952, pp. 145–147. Philadelphia, W. B. Saunders Co., 1953.
21. Dale, H. H. and Schuster, E. H. J.: A Double Perfusion Pump. J. Physiol. *14:* 356, 1928.
22. DeBakey, M.: Simple Continuous Flow Blood Transfusion Instrument. New Orleans M. & S. J. *87:* 386, 1934.
23. Karlson, K. E.: Ph.D. Thesis, 1952. University of Minnesota Library.
24. Reed, Raymond: Personal communication.
25. Dennis, C., Spreng, D. S. Jr., Nelson, C. E., Karlson, K. E., Nelson, R. M., Thomas, J. V., Eder, W. P. and Varco, R. L.: Development of a Pump-Oxygenator to Replace the Heart and Lungs. An Apparatus Applicable to Human Patients, and Application to One Case. Ann. Surg. *134:* 709, 1951.
26. Kirklin, J. F. and Wood, E. H.: Personal communication.
27. Geoghegan, T. and Lam, C. R.: The Mechanism of Death from Intracardiac Air and Its Reversibility. Ann. Surg. *138:* 351, 1953.
28. Fries, C. F. and Levowitz, B.: Studies on Cerebral Air Embolism. In press.
29. Kabat, H., Dennis, C. and Baker, A. B.: Recovery of Function Following Arrest of the Brain Circulation. Am. J. Physiol. *132:* 737, 1941.
30. Gibbon, J. H. Jr.: Personal communication.
31. Newman, M. H., Stuckey, J. H., Levowitz, B. S., Young, L. A., Dennis, C., Fries, C., Gorayeb, E. J., Zuhdi, M., Karlson, K. E., Adler, S. and Gliedman, M.: Complete and Partial Perfusion of Animal and Human Subjects with the Pump-Oxygenator. Surgery *38:* 30, 1955.

451 Clarkson Avenue
Brooklyn 3, New York